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IMPENDING AND REAL GANGRENE ASSOCIATED WITH DIABETES; CORRELATION OF MEDICAL AND SURGICAL EFFORT.

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It is well known that gangrene of the extremities is a fairly frequent complication in diabetes; not that the condition of diabetes itself necessarily gives rise to gangrene, but that in individuals suffering from this malady there is usually to be found an associated generalized arteriosclerosis which, together with the recognized lowered resistance of the tissues to infection, may be said to prepare the field for those circulatory disturbances of the extremities that eventuate in gangrene.

At the same time it must be admitted that fundamentally the diabetes controls the situation in so far that most of those who come to grief with gangrene are found either to have neglected the general condition or are sufferers from it in such intractable form that dietetic and therapeutic measures for its relief have been unavailing. At least this is so in my experience. It appears that the basic element dependent upon control of the diabetic condition is not so much a cessation of further development of the arteriosclerotic process in the extremity bloodvessels as it is a raised tissue resistance to infection and to the withstanding of the ischemia associated with occluded arteries; for in most cases that have come under my observation a halting of the arteriosclerotic process is of comparatively minor importance, since it has already proceeded to the point of almost total occlusion of the main terminal bloodvessel.[1] This leaves the limb to get along as best it may, with such collateral vascular channels as might have developed coincident with the gradual occlusion of these main vessels. The crux of the situation must therefore lie in the ability of the tissues to survive with a greatly diminished blood nourishment, and it is this ability which seems to be influenced by the diabetes.

That this is true is proved, I think, by the fact that in gangrenes other than those associated with diabetes it suffices in general to consider and treat the local condition alone, and if one is able to reëstablish the circulatory balance in a limb of precarious circulation, as is very frequently possible by means of rest, baths and gentle massage, the use of the electric vibrator and such other measures as one may employ in these difficult conditions[2] a successful issue may be expected. Not so in diabetes. Not once but many times have all my efforts to restore the circulatory balance gone to naught until the underlying condition could be brought under control. I refer particularly to those cases of only impending gangrene, cases which have not progressed to the stage of actual tissue death and where prompt measures might be expected to prevent it.

But in a way the same thing holds true for those who have an actual gangrene in that amputation will more than likely end disastrously, as is well known, unless at the time of operation the patient is sugar-free, and his acetone, diacetic acid, blood-sugar and carbonate findings have been brought into line. Or a better way of putting it would be to say that a patient's chances of surviving operation appear to be increased just in so far as his underlying diabetic malady is brought under control. It follows, therefore, that surgeons would do well to call to their aid physicians skilled in the treatment of this difficult disease, for it requires a special order of knowledge to deal with its various manifestations, a knowledge not usually possessed by surgeons.

This was forcibly brought home to me by a case (Mr. J. W.), which came under my care some years ago, of a man, aged sixty-eight years long a sufferer from diabetes, whose bloodvessels everywhere were of the pipe-stem variety. He had been under the constant supervision of Dr. E. J. Leopold, and in spite of occasional lapses had been carried along most successfully for a number of years, even to the point of surviving a desperate pneumonia. One winter, for some unaccountable reason, he became obsessed with the idea that he needed no further medical supervision. Being a hard drinker he indulged immoderately and totally neglected his usual dietary precautions—and with the inevitable result. When I saw him he had what looked to be a simple infection of his left great toe. Dr. Leopold was again in charge, but the patient's attitude was bad and his medical adviser was having poor success.

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[1] That is the main vessels of the lower leg and foot. It often happens that pulsation is felt in the popliteal artery, but invariably it is found to be one-half or three-quarters occluded by the sclerotic process. So the volume of blood passing through it must be very small.

[2] Pain in Threatened and Real Gangrene of the Extremities; Its Relief, Am. Jour. Med. Sc., 1922, **163**, 517.

I started out with the usual conservative measures of rest and moist, warm boric dressings, but the tissue broke down in spite of them. I then provided adequate drainage, but the tissues seemed to have little resistance, and although there was no pain at all connected with the affected area, more destruction ensued, and it was not long before the terminal joint was invaded. Dr. Leopold thereupon redoubled his efforts. Rigorous diet was enforced under adequate supervision and everything possible was done to stave off what looked like a spreading infection with gangrene. Dr. J. M. T. Finney saw the patient in consultation and advised that he be put to sleep, the joint opened, thoroughly cleaned out and all sloughing material removed. It was with a hopeless feeling that his advice was followed.

Just before this was done it was noted that the sugar content of the patient's urine was decreasing. Coincident with this it was further observed that while the roentgen-ray showed definite bone destruction in the joint, the surrounding tissue appeared to be taking on renewed vitality and that the inflammatory area had ceased to spread. The operation was carried out under nitrous-oxide gas anesthesia. For a few days the whole foot looked precarious, but actual gangrene did not supervene. After a while the condition seemed to improve some as the general condition of the patient began to respond to treatment. Shortly thereafter the diabetic process yielded, and following this the toe healed. The patient lived a fairly active life for several years after this, finally succumbing to a second attack of pneumonia.

I cite this case because it is a most unusual one and is a striking example of successful coöperation of surgical and medical effort. The whole period of surgical treatment was most tedious, and consumed four months.

Another case, equally striking was that of an elderly man, Mr. H. H. (a patient of Dr. Samuel Wolman), who also had long been a sufferer from diabetes. Always a difficult patient, he would at times go on a veritable carbohydrate debauch, and it was at the conclusion of one of these, in the spring of 1920, that he began to have pain in his right leg. This grew worse steadily until it became so acute and constant that it was agonizing for him to walk. Sleep was out of the question.

When I saw him, some two or three weeks after the onset, there was already present a slight but none the less definite atrophy of the calf mucles of the affected leg. When the man was on his feet the veins of his right leg stood out like whip-cords while the entire skin from the knee down assumed first a fiery red color, and then as he continued standing a purplish, ominous-looking dusky red. I have noticed this remarkable phenomenon many times in cases of threatened gangrene, and have been at a loss to explain it. The pain that accompanies it is excruciating. It looks as if the filled, tense veins would burst, and one cannot escape the feeling that the contained blood is surely obstructed in its outflow. Yet there is no obstruction demonstrable, for the moment the patient lies down the whole picture disappears, and if his leg is elevated a bit it assumes a pale, cadaveric appearance with great rapidity.

It looks rather as if at certain stages of a failing circulation in the extremities the innervation of the vessel walls becomes deranged to such extent that with the patient in the upright position there is a total loss of tone, with the resultant vein bulging with stagnant blood and the generalized phenomenon as noted.[3] This view is further supported by the fact that the affair may be purely temporary; as the circulatory balance is reëstablished by appropriate treatment the phenomenon becomes less and less pronounced; the pain on standing decreases, and finally the leg becomes normal in appearance both upon standing and lying down. In other words the vascular innervation once more becomes operative and the vessels regain their normal tone.

This is well illustrated by the story of the patient in question, as is my earlier statement that little can be accomplished without the physician's aid. I insisted immediately that Mr. H. remain in bed and be entirely off his feet. He was given the electric vibrator, hot and cold plunges to the foot and leg and such other measures as seemed indicated.[4] As the patient was in his own home the treatment was difficult and the dietary precautions nullified by his wilful excesses. His whole foot was exquisitely sensitive, and as the days progressed the picture as noted above became so exaggerated that finally I insisted that he go to the hospital for a final though, as it appeared, hopeless trial at saving the limb.

At the hospital the unexpected happened. Rigid dietary precautions were enforced, and within seventy-two hours the sugar in the urine began to clear while the man's whole aspect took on a different character. His blood sugar was 0.164 per cent. The electric vibrator, which is nothing but the gentlest form of massage, was carefully used, hot and cold plunges were regularly instituted every four hours, the leg was kept warm at all times, and in addition the patient was given a course of Ringer's solution.[5] It was not long before the pain began to subside. To make a long story short the whole picture cleared to such an extent that a few weeks later the patient was walking about as well as ever, and he has continued to do so.

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[3] I lay great stress upon this phenomenon in the diagnosis of threatened gangrene.

[4] Pain in Threatened and Real Gangrene of the Extremities; Its Relief, AM. JOUR. MED. SC., 1922, **163**, 517.

[5] Loc. cit.

Not all cases end so happily. Only too often it is not so much a question of saving the limb as the individual's life, for while diabetes itself is quite compatible with long life, diabetes plus a gangrenous limb is in all cases an extremely serious affair. Not that amputation is such a desperate ordeal in itself, but that any operative procedure of whatever magnitude is of serious import in the case of diabetes, the degree of seriousness depending for the most part apparently upon the state of carbohydrate metabolism derangement.

By way of illustration, I wish to cite three cases, each of which teaches a somewhat different lesson, though fundamentally all of them illustrate the close interrelation of surgery and medicine required for the proper handling of such cases.

The first is that of Mr. M. S., aged sixty years, a patient of Dr. T. B. Futcher. Long a diabetic, he arrived in Baltimore from the South in a profound state of acidosis. Some two or three weeks previous he began to have a soreness in his right foot, for which his medical adviser prescribed hot-water bottles. Several superficial burns on the toes resulted, and after that the dorsum of the foot became red and inflamed, and reddish streaks made their appearance above the ankle. It was then that he came to Baltimore.

Upon his arrival, April 2, 1921, he was critically ill, vomiting frequently. His urine was loaded with sugar, 2+ per cent, and also with diacetic acid and acetone, +++. His blood sugar was 0.25 per cent and his blood carbonate 39 vol. per cent.[6] His foot was obviously infected, and it seemed to have an accumulation of pus just under the skin of the dorsum, while two of his toes were already gangrenous. There was, however, no outspoken lymphangitis, and the patient's temperature was hardly elevated. So in view of his precarious general state, surgical intervention was postponed until medical measures at least could be gotten under way.

Within a few days the toxic symptoms began to subside, so that it was possible to incise and drain the dorsum of the foot. The operation was done under local anesthesia with the patient in his bed. Quantities of foul-smelling, grayish-black pus, such as is characteristically found in the tissue destruction of gangrene, were released. Following this the whole dorsum of the foot gradually became gangrenous and at each dressing that part which was obviously destroyed was removed. The two toes were removed in the same way, and as a third toe wilted it too was removed—piecemeal.

It was necessary to do this, I felt, because the accumulation of necrosed and sloughing material, with its accompanying foul-smelling liquefaction, was so great that to leave it meant that a certain amount of absorption of toxic matter must result. To have removed

[6] I am indebted to Dr. Louis Sacks, resident surgeon at the Hebrew Hospital, for much aid in the preparation of this article.

the foot—as was obviously indicated— was out of the question at this time, because the patient's general state remained so desperate as to preclude giving him an anesthetic or carrying out any operation of magnitude. But we were particularly fortunate in this case,[7] because the individual in question never suffered the slightest pain from his rapidly decaying foot. This was one of the most remarkable cases in this respect I have ever encountered. Thus by keeping well away from the line of demarcation, which was progressive, all excision of tissue was accomplished without pain and without anesthesia of any kind.

Under the constant watchfulness of Dr. Futcher, Mr. S. gradually improved. His urine revealed less and less sugar until, weeks after his admission, it finally became sugar-free. His acetone and diacetic acid, however, were very refractory, being +++ for the acetone and + for the diacetic acid. It seemed impossible to get his blood sugar below 0.21 per cent, in spite of repeated starvation days and the most rigidly careful diet on other days.

During these trying weeks there was the widest possible opening in the foot for drainage, the skin, subcutaneous tissue, extensor muscles and tendons having been removed. But the interosseous muscles were becoming affected and sloughing material was constantly oozing up between the metatarsal bones. It then occurred to me that even though the patient's temperature was running about normal, absorption was going on nevertheless, and that this was the reason for the failure of urinary and blood findings to approach normal. Dr. Futcher and I discussed this possibility and the proposition that as long as the affected leg remained unamputated the diabetic condition of the patient probably would not show further improvement. I must admit that, surgically speaking, the man's wounds were so wide open that absorption of any serious surgical significance seemed out of the question. My only ground for thinking that there was any absorption at all was merely the fact that the most intensive efforts of the medical men to improve the diabetic condition after it had reached a certain point were without avail. Our combined experience, however, in regard to this matter was rather meager, and the literature contains little or nothing concerning it.[8] It seemed a marvelous opportunity to shed some light on this point by proceeding with the amputation—and the temptation was great—but the patient's condition was such that it would have been unwise to carry out any operation without exhausting every possible means of bringing his laboratory (blood and urine) findings to normal. We therefore continued our efforts in this direction even though the gangrenous process continued to advance. I might add that the circulation in the affected leg was quite satisfactory, the patient had his normal femoral and popliteal pulses, and that such granulation tissue as formed bled with remarkable ease. In other words the spread of the gangrene was not dependent upon a circulatory failure but obviously upon a lowered resistance of the tissues to infection and to ischemia. Lest there might be some skepticism on this point, I would add that not only was the circulation quite satisfactory, but there was no edema of the foot, ankle or leg which might have interfered with a circulation that was adequate. But toward the seventh week under our care the sole of the foot began to redden. A little later it became obvious that the process had broken through the plantar fascia from above (as was to be expected), and if prompt measures were not taken a fulminating gangrene might result. This, of course, was to be avoided at all hazards. At this time the urinary and blood findings were as follows:

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[7] The gangrenes of diabetes are more prone to be of the painless variety than other gangrenes, though just why this should be I do not know.

[8] Ordinarily, if a patient is absorbing from a surgical wound, one feels that the drainage is insufficient and that this will be manifested by pain, swelling and elevation of temperature.

May 18, 1921. Urine: Glucose, 0.7 per cent (14.7 gm.); acetone, +++; diacetic, +; albumin, +. Blood sugar, 0.24 per cent.

That is they still had not reached normal. The opportunity to discover the relation of absorption from gangrenous tissue to continued carbohydrate derangement in so far as a single example could teach was within our grasp. We had played fair with the patient from an actual surgical standpoint by carrying him along without operation until his leg actually began to threaten his life.

Therefore, on May 19, 1921, under nitrous oxide gas and some ether, a hurried amputation was done at the midcalf. The patient reacted very well, and, with the exception of one small area on the outer side of the stump, the wound healed without difficulty. As we had hoped, the postoperative course of the diabetes justified fully the view held that the failure of the carbohydrate derangement to yield entirely to treatment was due purely to the absorption taking place. At least there is no other explanation for the fact that within about two weeks after the operation, June 14, 1921, the urinary findings came down to normal. The blood sugar dropped to 0.20 per cent and continued to decrease, reaching normal one week before discharge from the hospital, July 13, 1921, some three and a half months after his admission.

At this time he was on an extremely liberal diet. Daily diet the week of discharge from the hospital was as follows:

Morning: Lister biscuits, 2; peach, 1; eggs, 2; milk, 270 cc; coffee, 250 cc; butter, 10 gm.

Afternoon: Orange, 100 gm.; broth, 200 cc; beef, 100 gm.; squash, 150 gm.; tea, 200 cc; cucumber, 100 gm.; potato, 100 gm.; lister biscuit, 2. Ice cream: Milk, 150 cc; cream, 160 cc; saccharine, $\frac{3}{4}$ gr.

Evening (supper): Cottage cheese, 50 gm.; beef, 100 gm.; squash, 150 gm.; tomato, 75 gm.; lettuce, 25 gm.; milk, 300 cc.; coffee, 250 cc; lister biscuits, 2.

His general condition was all that could be desired and his carbohydrate tolerance had actually been raised to really respectable limits.

This case, then, is an illustration of the principle that in certain instances our efforts must be directed not so much toward saving the limb as saving the patient's life, and that even this at times is most problematical.

For example, just recently I had under my care a woman (Mrs. K.), for many years a sufferer from diabetes, who began to have trouble with her right leg. She was seen by Dr. Helfgott, who advised that she come to the hospital for treatment. His advice was ignored and he lost sight of her for some three months. At the end of that time the patient again came under his observation, but by that time her whole right foot had become gangrenous.

I saw her in consultation April 8, 1921, and had her sent to the hospital immediately. The patient's whole foot was decayed, the toes were hanging by shreds of tissue and in several areas where the skin was broken great quantities of pus could be expressed from the sole of the foot. The gangrenous process was gradually spreading up the ankle and the lower leg was edematous. Her urinary and blood findings at this time were as follows:

Urine: Sugar, ++++; acetone, ++++; diacetic acid, +.

Blood: Blood sugar, 0.4 per cent; blood carbonate, 48.6 vol. per cent.

Dr. Leopold, the attending physician at the Hebrew Hospital, felt that if operation could be postponed a few days it might be possible to do much in the way of improving the patient's condition and rendering the operative outcome more certain. Accordingly the foot was dressed in wet boric compresses, and from day to day the gangrenous material was removed. This patient suffered so much pain at all times that it was difficult to do much with her. For some ten days this coöperative method of medical and surgical treatment was continued and the patient showed some favorable response. The findings were as follows:

Urine: Glucose, 0; acetone, ++; diacetic acid, +.

Blood: Blood sugar ranged from 0.396 per cent to 0.48 per cent.

At this time, however, the edema of the lower leg was becoming more pronounced. It spread up the leg and definite lymphangitic streaks made their appearance chiefly along the internal saphenous vein. In other words it became obvious that the infection was progressing and that the patient's life depended upon prompt surgical interference. Accordingly a midthigh amputation was carried out. At the time of the operation the patient was in much better physical condition than upon her admission. Her temperature was down and she was practically sugar-free. Dr. Leopold and I felt that she would do fairly well after the operation, but we were disappointed. During the first twenty-four hours she was in desperate shape, but by the use of intravenous sodium bicarbonate she was tided over. For three days thereafter, April 23, 1921, she was showing improvement, and we began to feel hopeful. Her blood sugar dropped from 0.48 per cent to 0.34 per cent. Then with but little warning, some twenty-four hours after this, the patient suddenly went into a coma and died.

This case is an illustration of the difficulties that may be encountered at any time in the treatment of gangrene, namely, that a gangrene which is quiescent may suddenly become fulminating no matter what the condition of the patient. Under these circumstances, of course, operation is the lesser of two evils, and the patient must take the chance.

In the case of a third patient, Mr. S., aged fifty-four years, the conditions were even more deplorable. Not only was there the diabetic condition with a fulminating gangrene of the leg present, but in addition there was active pulmonary tuberculosis of long standing with cavities in both lungs. This involved state of affairs existed when I first saw the individual, the case having been treated on the outside for several months by others. Dr. Charles Austrian was invited to take over the medical side of the case, and at his suggestion a midthigh amputation was carried out under spinal anesthesia. The operation was done as an emergency at night; such was the danger from the rapidly advancing gangrene.

The patient was a large, fat, flabby man, definitely toxic. He had been under a fairly rigid diabetic regimen for some time at home, and as a result his urine was practically normal on admission. His blood sugar was 0.25 per cent and blood carbonate 33 vol. per cent. Despite the unfavorable outlook (to our surprise and relief) he stood the operation unusually well. With the exception of an annoying hiccough, that persisted for about forty-eight hours, his convalescence was uninterrupted. His carbohydrate metabolism was rapidly controlled, with the result that prior to his discharge from the hospital his diet was almost as liberal as that of a normal individual; his urine was sugar—, acetone—, and diacetic acid-free; his blood sugar was 0.117 per cent. and blood carbonate 45 vol. per cent. His carbohydrate tolerance had been raised to really respectable proportions.

These various cases are illustrations of what may be accomplished by closely allied medical and surgical forces when arrayed against a really dangerous condition. I have taken particular pains to emphasize this feature because it has been my experience that physicians tend to handle the surgical complications of diabetes too much by themselves, thereby frequently losing the opportunity for constructive measures. This is the one side. On the other side I find that the surgeon, when once he is consulted, is too prone to disregard the medical phase of the situation in his efforts to overcome the surgical complaint. How much better it would be for all concerned if there were an intelligent coördination of effort from the very start.

THE PREVENTION OF SIMPLE GOITER IN MAN.[1]

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To understand why anyone should undertake a goiter survey of a whole community for the purpose of establishing a principle of prevention by a simple and practical method, it is necessary to study the literature of goiter with this idea in view. For the literature, while rich in statements regarding the distribution of goiter, the pathology of the thyroid gland, methods of medical and surgical treatment, hereditary tendencies and etiology, has little indeed to offer regarding the *prevention* of goiter.

A survey for merely determining the incidence of goiter in the different localities and cities of this portion of the Great Lakes basin would have been unnecessary. There is an abundance of scientific data giving in general the geographic distribution of endemic goiter throughout the world. Surveys of various communities in Europe have been made and the scientific data of the last century has so emphasized the sociologic and economic importance of endemic goiter, cretinism and deaf-mutism that national commissions have been appointed by some of the countries of Europe to study this problem for the purpose of finding some method of relief.

For ten years preceding the beginning of our work in Akron, Marine and Lenhart, working in the department of experimental medicine of the Western Reserve University, had been showing the ease with which endemic goiter could be prevented. The results of laboratory experiments and demonstration in animals, however convincing, must be applied to man for final proof of their prophylactic or therapeutic value. The prevention of goiter in man was yet to be proven. Therefore, with Dr. David Marine, I undertook to establish in man the applicability of the work of Marine and Lenhart as summed up in their statement that "simple goiter is the easiest of all known diseases to prevent."

Definition and History of Endemic Goiter. The term goiter means hypertrophy of the thyroid gland. The term as used in this paper refers only to what is known as *simple* or *endemic goiter* and does not include the so-called exophthalmic goiter.

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[1] Presented as a thesis for the degree of Master of Arts in Medicine, Western Reserve University, June, 1921.